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10/088,538	06/10/2002	Thomas N. Masters	38151/203996	6926

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EXAMINER	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/088,538
Filing Date: June 10, 2002
Appellant(s): MASTERS, THOMAS N.

Ernest B. Lipscomb,III
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 01/09/2006 appealing from the Office action mailed 09/09/2005.

(1) Real Party in Interest

The brief has acknowledged the real party in interest in this appeal is Charlotte-Mecklenburg Hospital Authority d/b/a Carolinas Medical Center, the assignee of the above-referenced patent application.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

No amendment after final has been filed.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(8) Evidence Relied Upon

5,693,462	RAYMOND	12-1997

Massoudy, S. et al., "Cardioprotection by Cyclosporine A in Experimental Ischemia and Reperfusion-Evidence for a Nitric Oxide-dependent Mechanism Mediated by Endothelin", J. Mol. Cell. Cardiol., Vol. 29, pp. 535-544, 1997.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6, 7 and 9-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Massoudy et al. (*J. Mol. Cell. Cardiol.* 29, 535-544) in view of Raymond (USPN 5693462).

Massoudy et al. teaches that cyclosporine A acts as a cardioprotective agent in ischemia and reperfusion (Abstract). Cyclosporine A, in concentrations of 0.8 μm in Krebs-Henseleit buffer, was shown to significantly prevent the loss of post-ischemic cardiac function in isolated hearts (p. 536, col. 2, last ¶; p. 539, col. 2, 1st ¶). The reference does not teach the preferred concentration.

Raymond teaches the components of the Krebs-Henseleit buffer as comprising those components as instantly claimed (col. 4, lines 15-33).

It would have been obvious, absent a showing of unexpected results, to one of ordinary skill in the art at the time of the invention to treat an isolated heart with a composition comprising the claimed amount of cyclosporine A because Massoudy et al. teaches that such compositions are useful at preserving the heart and "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

It is noted that it would have been obvious to one of ordinary skill in the art at the time of the invention to utilize the compositions of Massoudy et al. in treating a heart prior to transplantation because, as taught by Massoudy et al., such a treatment significantly prevents the loss of post-ischemic cardiac function. Accordingly, one would have been motivated to treat hearts awaiting transplantation to preserve the cardiac function thereof.

It is also noted that the methods of Massoudy et al. and those as instantly claimed are both directed to preserving of a heart. Accordingly, the composition rendered obvious by the combined references would obviously block apoptosis because the same composition administered for the same purpose will obviously function via the same mechanism, whether or not that mechanism is disclosed in the prior art.

(10) Response to Argument

The applicant's have argued that amending claim 6 to read "consisting essentially of" overcomes the Raymond patent as set forth in the 103(a) rejection of

record. Applicants state that Raymond teaches a preservation solution for preserving and storing organs comprising (a) an isotonic solution; (b) an amiloride-containing compound; (c) adenosine; and (d) water. Further the applicants set forth that the Raymond patent does not teach the use of cyclosporin A in the methods or medicaments disclosed therein. Without admitting to the validity of the applicants statements the examiner respectfully points out that the Raymond patent has been utilized only to demonstrate the components of the Krebs-Henseleit buffer (see 9/9/2005 Final Office Action page 2) and to illustrate that the Krebs-Henseleit buffer comprises the identical components as currently claimed in claims 10 and 14. Further Raymond is not the primary art of record as the rejection is listed as Massoudy in view of Raymond.

Massoudy et al. teaches the use of cyclosporine A as a cardioprotective agent in ischemia and reperfusion in isolated hearts (p. 536, col. 2; p.539, col2). Further Massoudy teaches the use of cyclosporine A in concentrations of 0.8μM in Krebs-Henseleit buffer. The examiner respectfully points out that as noted above the components of the Krebs-Henseleit buffer are identical to the components currently claimed and explicitly set forth in claims 10 and 14.

Applicant argues "cyclosporin A is used to concentrations of 0.08 μM and 0.8 μM which is the effective plasma level required in patients after heart transplantation." This argument is not persuasive because, as discussed above, Massoudy et al. teaches the treatment of *isolated* hearts.

Applicant argues, "[t]he lower level of CSA used in the present invention is **at least three times** the amount of CSA disclosed in Massoudy *et al.*" This argument is

not persuasive absent a showing of unexpected results because it would have been obvious to one of ordinary skill in the art that increasing the concentration would be at least as effective as the lower concentrations of Massoudy et al. Furthermore, Massoudy et al. uses the concentrations as examples in experimentation. The skilled artisan would not recognize these as limitations on the concentrations useful in the preparation of a composition for the preservation of a heart. It is well established that consideration of a reference is not limited to the preferred embodiments or working examples, but extends to the entire disclosure for what it fairly teaches, when viewed in light of the admitted knowledge in the art, to a person of ordinary skill in the art. *In re Boe*, 355 F.2d 961, 148 USPQ 507 (CCPA 1966); *In re Lamberti*, 545 F.2d 747, 19USPQ 279 (CCPA 1976); *In re Fracalossi*, 681 F.2d 792, 215 USPQ 569 (CCPA 1982); *In re Kaslow*, 707 F.2d 1366, 217 USPQ 1089 (Fed. Cir. 1983).

Applicant argues that preventing apoptosis has nothing to do with the findings of Massoudy et al., specifically with the nitic oxide-dependent mechanism impeded by endothelin. The applicant's provide no comparative evidence showing that such a mechanism could not be useful in preventing apoptosis and fail to provide an alternate rationale for why cyclosporin A would prevent apoptosis. Further the claims are drawn to methods of blocking apoptosis and not to preventing apoptosis and the claims clearly are drawn to perfusion of an isolated heart awaiting transplantation (meaning the heart has been isolated, removed, blood flow ceased (ischemia) and then perfused with the cyclosporin A isotonic water solution).

The applicant argues that Massoudy et al. is silent about the effects on an isolated heart preserved in the isotonic solutions disclosed and thus Massoudy et al. does not suggest that the isotonic solution therein disclosed would be particularly suited for solutions for preserving and storing a heart awaiting transplantation. The examiner respectfully disagrees. Massoudy et al. clearly teaches the use of cyclosporine A in Krebs-Henseleit buffer in the treatment of ischemia-reperfusion in ***isolated*** hearts. As hearts awaiting transplantation are isolated at some point and stored and as the Kreb-Henseleit buffer is an accepted transplantation buffer for use in handling organs for transplantation (Raymond), and as the Krebs-Henseleit buffer is identical to the isotonic solution as currently claimed in claims 10 and 14 it is clear that the Massoudy et al. cyclosporin A solutions are suitable for storing isolated hearts awaiting transplantation.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Leonard Williams

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